UK National Screening Committee

Screening for Haemochromatosis

12 October 2016

Aim

1. To ask the UK National Screening Committee (UK NSC) to make a recommendation, based upon the evidence presented in this document, whether or not screening for Haemochromatosis meets the UK NSC criteria to support the introduction of a population screening programme.

   This document provides background on screening for haemochromatosis.

Current recommendation

2. The 2009 review of screening for haemochromatosis concluded that systematic screening of adults in the general population did not meet the UK NSC criteria and the committee did not recommend its introduction.

   Although there natural history of hereditary haemochromatosis was not wholly understood, the reported penetrance of HFE genotypes (the faulty HFE gene) was low. By offering screening, many people would be informed of the condition and be worried unnecessarily as the condition may not develop. Furthermore that was a lack of consensus as to what an effective screening strategy would be for detecting the disease. This was particularly the case for severe outcomes. In addition an effective screening strategy had not been identified and the effectiveness of venesection (phlebotomy) to reduce blood-iron levels in screen detected populations was uncertain.

Review

3. This review was undertaken by Ottawa Hospital Research Institute, in accordance with the triennial review process. http://legacy.screening.nhs.uk/haemochromatosis

4. This review focuses on whether any studies have been published which might improve estimates of penetrance and to establish whether any studies have been published which identify a suitable and reliable screening strategy for the UK population.

5. The conclusion of this review is to reaffirm the UK NSC recommendation not to screen for haemochromatosis in the UK adult population. The reasons remain unchanged from the previous review:

    a. A small number of studies were found addressing the penetrance of HFE genotypes and these reported findings that were consistent with those reported in the previous review. **Criterion 2 not met**

    b. Only one study was found which reported on a screening strategy and this was considered insufficient in terms of establishing a suitable screening strategy. **Criterion 6 not met**

Consultation

6. A three month consultation was hosted on the UK NSC website. Direct emails were sent to stakeholders of whom 11 organisations were contacted directly. **Annex A**

7. Responses were received from the following two stakeholders; The Royal College of Pathologists, and Genetic Alliance UK. All comments are in **Annex B**, below.

    Both responses agreed with the conclusion of the review.

Recommendation

8. The committee is asked to approve the following recommendation:
    A systematic population screening programme for haemochromatosis is not recommended.

    Based on the 22 UK NSC criteria set to recommend a population screening programme, evidence was appraised against the following two criteria:

Criteria	Met / Not met
The Condition	

2	The epidemiology and natural history of the condition, including development from latent to declared disease, should be adequately understood and there should be a detectable risk factor, disease marker, latent period or early symptomatic phase.	Not met ✘
The Test		
6	The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.	Not met ✘

Annex A

List of organisations contacted:

1. British Association for Study of the Liver
2. British Liver Nurses' Forum
3. The British Liver Trust
4. The British Society for Haematology
5. British Society of Gastroenterology
6. Faculty of Public Health
7. The Haemochromatosis Society
8. Royal College of General Practitioners
9. Royal College of Pathologists
10. Royal College of Physicians
11. Royal College of Physicians of Edinburgh

The Royal College of Pathologists
Pathology: the science behind the cure

Response from the Royal College of Pathologists to Consultation on Screening for Haemochromatosis

The Royal College of Pathologists' written submission

July 2016

1 About the Royal College of Pathologists

1.1 The Royal College of Pathologists (RCPath) is a professional membership organisation with charitable status. It is committed to setting and maintaining professional standards and to promoting excellence in the teaching and practice of pathology. Pathology is the science at the heart of modern medicine and is involved in 70 per cent of all diagnoses made within the National Health Service. The College aims to advance the science and practice of pathology, to provide public education, to promote research in pathology and to disseminate the results. We have over 10,000 members across 19 specialties working in hospital laboratories, universities and industry worldwide to diagnose, treat and prevent illness.

1.2 The Royal College of Pathologists comments were made by Fellows of the College during the consultation which ran from 18th May 2016 until the 17th June 2016 and collated by Dr Rachael Liebmann, Registrar.

2 CONTENTS

2.1 College Fellows considered this to be a well-written and evidenced document.

2.2 Also for clarity the executive summary makes clear that there is a lack of sufficient high quality evidence and therefore the authors conclude there is no point in changing the present recommendation. It would aid understanding if the authors stated clearly what the present recommendation is in the executive summary.

2.3 The comment was made that the authors should highlight their focus on HFE-related hereditary haemochromatosis (type 1), which is relevant to 90% of cases. Current practise uses a much more detailed classification of the disease including juvenile disease (types 2a and 2b) and types 3 and 4 (mutations in the TFR2 and FPN genes). It was proposed that the committee need to clarify that these non-HFE types of HH were outside the scope of this document.

UK National Screening Committee

Name:	Alastair Kent OBE	**Email address:**	xxxx xxxx
Organisation (if appropriate):	Genetic Alliance UK		
Role:	Director		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes ☒ **No** ☐

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
General		We support the conclusion of the review that at this time general population screening for haemochromatosis in adults in not appropriate. The review focuses on the uncertainties of evidence relating to penetrance figures and natural history rather than the implications of what is known. However, numerous studies

		suggest that a minority of those homozygous for the most common HH genotype will progress to iron overload, and even fewer to symptomatic disease. This low penetrance and uncertainty means that either a genotype based general population screening programme or a phenotype based general population screening programme based on blood iron or serum ferritin levels would lead to high levels of false positives, causing unnecessary anxiety and distress. Until or unless a test is developed better able to predict which patients will develop symptoms general population screening is not appropriate. However, we wish to support our member organisation the Haemochromatosis Society in raising concerns about current implementation of cascade screening. Best practice guidelines in both Europe (from European Association for the Study of the Liver) and internationally strongly recommend cascade genetic testing of first degree relatives of patients with symptomatic disease, as well as case finding in high risk groups showing relevant symptoms. This approach is both more cost effective and more likely to achieve the goal of early diagnosis. However, we are informed that this frequently does not take place.